QR 180.H85
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1: Hum Immunol 1999 Jul;60(7):583-90 Related Articles, Links

FULL-TEXT ARTICLE

NOD background genes influence T cell responses to GAD 65 in HLA-DQ8 transgenic mice.

Abraham RS, Wilson SB, de Souza NF Jr, Strominger JL, Munn SR, David CS.

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The major histocompatibility complex (MHC) genes play a significant role in the predisposition to insulin-dependent diabetes mellitus or type 1 diabetes. HLA-DQ8 (DQB1*0302, DQA 1*0301) genes have been shown to have the highest relative risk for human type 1 diabetes. To develop a "humanized" mouse model of diabetes, HLA-DQ8 was transgenically expressed in mice lacking endogenous class II genes. Since non-MHC background genes of the NOD influence the disease process, AP"/DQ8 mice were mated with the NOD strain and backcrossed to generate Abeta degree/DQ8/NOD mice. These mice have DQ8 as the sole MHC class II restriction element with NOD background genes at the N 2 generation. The DQ8 transgenic mice were used to identify T cell epitopes on glutamic acid decarboxylase (GAD 65), an important putative autoantigen in type 1 diabetes. The NOD background genes strongly influenced antigen processing, that is, different T cell epitopes were generated from the processing of GAD 65 in vivo in the Abeta degree/DQ8 and in the Abeta degree/DQ8/NOD mice.

PMID: 10426275 [PubMed - indexed for MEDLINE]

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DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L14	Abraham-roshini-S$.in.	0	L14
L13	David-chella-S$.in.	1	L13
L12	(transgenic adj mouse) same (DR3)	6	L12
L11	(transgenic adj mouse) same (I-Ealpha)	1	L11
L10	L9 and (DRab and DQab)	2	L10
L9	L8 and (DR3)	27	L9
L8	L2 or L5 or L6 or L7	1637	L8
L7	(SCID adj (mouse or mice))	1630	L7
L6	((CD3 or Ig) adj knockout)	2	L6
L5	L4 and (TCR adj knockout)	1	L5
L4	(transgenic adj mouse) same (TCR)	129	L4
L3	(transgenic adj mouse) same (RAG-2)	12	L3
L2	(transgenic adj mouse) same (RAG-?)	13	L2
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1: Hum Immunol 2002 Nov;63(11):987-99

Related Articles, Links

FULL-TEXT ARTICLE

Modulation of insulitis and type 1 diabetes by transgenic HLA-DR3 and DQ8 in NOD mice lacking endogenous MHC class II.

Kudva YC, Rajagopalan G, Raju R, Abraham RS, Smart M, Hanson J, David CS.

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To evaluate the contributions of DR3 and DQ8 to the etiopathogenesis of type 1 diabetes in a diabetes-predisposing milieu, we developed human leukocyte antigen (HLA) transgenic mice on the nonobese diabetic (NOD) background in the absence of the endogenous class II molecule, I-A(g7) and studied the incidence of both spontaneous and experimental (induced) autoimmune diabetes. Transgenic expression of HLA-DR3 and -DQ8 (either alone or in combination) did not confer susceptibility to spontaneous or cyclophosphamide-induced type 1 diabetes. Expression of I-A(g7) was mandatory for development of spontaneous or cyclophosphamide-induced diabetes. However, multiple low doses of streptozotocin could induce diabetes in all groups of mice independent of the class II molecules expressed. In unmanipulated mice, only islets from I-A(g7+/+) mice revealed significant intra-islet infiltration. Although a characteristic peri-insulitis/peri-ductulitis was present in Abeta(0)/NOD mice, islets from DR3, DQ8 and DR3 x DQ8 double transgenic mice demonstrated significantly less infiltration. In conclusion, transgenic expression of HLA-DR3 and -DQ8 associated with predisposition to type 1 diabetes alone is not sufficient to induce spontaneous diabetes in NOD mice lacking endogenous class II molecules.

PMID: 12392851 [PubMed - in process]